NOVAREL - chorionic gonadotropin injection
Ferring Pharmaceuticals Inc.

DESCRIPTION

Human chorionic gonadotropin (HCG), a polypeptide hormone produced by the human placenta, is composed of an alpha and a beta sub-unit. The alpha sub-unit is essentially identical to the alpha sub-units of the human pituitary gonadotropins, luteinizing hormone (LH) and follicle-stimulating hormone (FSH), as well as to the alpha sub-unit of human thyroid-stimulating hormone (TSH). The beta sub-units of these hormones differ in amino acid sequence.
Chorionic Gonadotropin is a water soluble glycoprotein derived from human pregnancy urine. The sterile lyophilized powder is stable. When reconstituted with Bacteriostatic Water for Injection preserved with benzyl alcohol 0.9%, the solution should be refrigerated and used within 30 days.
Each vial contains:
Chorionic Gonadotropin **10,000** USP Units, Mannitol 100 mg, Dibasic Sodium Phosphate 16 mg, and Monobasic Sodium Phosphate 4 mg.

CLINICAL PHARMACOLOGY

The action of HCG is virtually identical to that of pituitary LH, although HCG appears to have a small degree of FSH activity as well. It stimulates production of gonadal steroid hormones by stimulating the interstitial cells (Leydig cells) of the testis to produce androgens and the corpus luteum of the ovary to produce progesterone. Androgen stimulation in the male leads to the development of secondary sex characteristics and may stimulate testicular descent when no anatomical impediment to descent is present. This descent is usually reversible when HCG is discontinued. During the normal menstrual cycle, LH participates with FSH in the development and maturation of the normal ovarian follicle, and the mid-cycle LH surge triggers ovulation. HCG can substitute for LH in this function. During a normal pregnancy, HCG secreted by the placenta maintains the corpus luteum after LH secretion decreases, supporting continued secretion of estrogen and progesterone, and preventing menstruation. HCG HAS NO KNOWN EFFECT ON FAT MOBILIZATION, APPETITE OR SENSE OF HUNGER, OR BODY FAT DISTRIBUTION.

INDICATIONS AND USAGE

HCG HAS NOT BEEN DEMONSTRATED TO BE EFFECTIVE ADJUNCTIVE THERAPY IN THE TREATMENT OF OBESITY. THERE IS NO SUBSTANTIAL EVIDENCE THAT IT INCREASES WEIGHT LOSS BEYOND THAT RESULTING FROM CALORIC RESTRICTION, THAT IT CAUSES A MORE ATTRACTIVE OR “NORMAL” DISTRIBUTION OF FAT, OR THAT IT DECREASES THE HUNGER AND DISCOMFORT ASSOCIATED WITH CALORIE-RESTRICTED DIETS.

1. Prepubertal cryptorchidism not due to anatomic obstruction. In general, HCG is thought to induce testicular descent in situations when descent would have occurred at puberty. HCG thus may help to predict whether or not orchiopexy will be needed in the future. Although, in some cases, descent following HCG administration is permanent, in most cases the response is temporary. Therapy is usually instituted between the ages of 4 and 9.

2. Selected cases of hypogonadotropic hypogonadism (hypogonadism secondary to a pituitary deficiency) in males.

3. Induction of ovulation and pregnancy in the anovulatory, infertile woman in whom the cause of anovulation is secondary and not due to primary ovarian failure, and who has been appropriately pretreated with human menotropins.

CONTRAINDICATIONS

Precocious puberty, prostatic carcinoma or other androgen-dependent neoplasm, prior allergic reaction to HCG. HCG may cause fetal harm when administered to a pregnant woman. Combined HCG/PMS (pregnant mare’s serum) therapy has been noted to induce high incidences of external congenital anomalies in the offspring of mice, in a dose-dependent manner. The potential extrapolation to humans has not been determined.

WARNINGS

HCG should be used in conjunction with human menopausal gonadotropins only by physicians experienced with infertility problems who are familiar with the criteria for patient selection, contraindications, warnings, precautions, and adverse reactions described in the package insert for menotropins. The principal serious adverse reactions during this use are: (1) Ovarian hyperstimulation, a syndrome of sudden ovarian enlargement, ascites with or without pain, and/or pleural effusion; (2) Enlargement of preexisting ovarian cysts or rupture of ovarian cysts with resultant hemoperitoneum; (3) Multiple births, and (4) Arterial thromboembolism.
The recommended diluent for reconstitution is Bacteriostatic Water for Injection preserved with benzyl alcohol 0.9%. Benzyl alcohol has been reported to be associated with a fatal “Gasping Syndrome” in premature infants.

PRECAUTIONS

General

1. Induction of androgen secretion by HCG may induce precocious puberty in patients treated for cryptorchidism. Therapy should be discontinued if signs of precocious puberty occur.

2. Since androgens may cause fluid retention, HCG should be used with caution in patients with cardiac or renal disease, epilepsy, migraine, or asthma.

Drug/Laboratory test

HCG can crossreact in the radioimmunoassay of gonadotropins, especially luteinizing hormone. Each individual laboratory should establish the degree of crossreactivity with their gonadotropin assay. Physicians should make the laboratory aware of patients on HCG if gonadotropin levels are requested.

Carcinogenesis, Mutagenesis, Impairment of Fertility

There have been sporadic reports of testicular tumors in otherwise healthy young men receiving HCG for secondary infertility. A causative relationship between HCG and tumor development in these men has not been established. Defects of forelimbs and of the central nervous system, as well as alterations in sex ratio, have been reported in mice on combined gonadotropin and HCG regimens. The dose of gonadotropin used was intended to induce superovulation. No mutagenic effect has been clearly established in humans. Fertility—see “Indications and Usage.”

Pregnancy

Teratogenic Effects

Category X: See “Contraindications” section. Combined HCG/PMS (pregnant mare’s serum) therapy has been noted to induce high incidences of external congenital anomalies in the offspring of mice, in a dose-dependent manner. The potential extrapolation to humans has not been determined.

Nursing Mothers

It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when HCG is administered to a nursing woman.

Pediatric Use

Safety and effectiveness in children below the age of 4 have not been established.

ADVERSE REACTIONS

(See WARNINGS) Headache, irritability, restlessness, depression, fatigue, edema, precocious puberty, gynecomastia, pain at the site of injection. Hypersensitivity reactions both localized and systemic in nature, including erythema, urticaria, rash, angioedema, dyspnea and shortness of breath, have been reported. The relationship of these allergic-like events to the polypeptide hormone or the diluent containing benzyl alcohol is not clear.

DOSAGE AND ADMINISTRATION

(Intramuscular Use Only): The dosage regimen employed in any particular case will depend upon the indication for use, the age and weight of the patient, and the physician’s preference. The following regimens have been advocated by various authorities.
Prepubertal cryptorchidism not due to anatomical obstruction:
(1) 4,000 USP Units three times weekly for three weeks.
(2) 5,000 USP Units every second day for four injections.
(3) 15 injections of 500 to 1,000 USP Units over a period of six weeks.
(4) 500 USP Units three times weekly for four to six weeks. If this course of treatment is not successful, another is begun one month later, giving 1,000 USP Units per injection.
Selected cases of hypogonadotropic hypogonadism in males:
(1) 500 to 1,000 USP Units three times a week for three weeks, followed by the same dose twice a week for three weeks.
(2) 4,000 USP Units three times weekly for six to nine months, following which the dosage may be reduced to 2,000 USP Units three times weekly for an additional three months.
Induction of ovulation and pregnancy in the anovulatory, infertile woman in whom the cause of anovulation is secondary and not due to primary ovarian failure and who has been appropriately pre-treated with human menotropins (See prescribing information for menotropins for dosage and administration for that drug product).
5,000 to 10,000 USP Units one day following the last dose of menotropins. (A dosage of 10,000 USP Units is recommended in the labeling for menotropins).
Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit.

HOW SUPPLIED

Chorionic Gonadotropin for Injection, USP, is available as individually packaged vials containing 10,000 USP Units per vial (NDC 55566-1501-0).

Store dry product at controlled room temperature 15° - 30° C (59° - 86° F).

AFTER RECONSTITUTION WITH BACTERIOSTATIC WATER FOR INJECTION PRESERVED WITH BENZYL ALCOHOL 0.9%, REFRIGERATE THE PRODUCT AT 2° - 8° C (36° - 46° F) AND USE WITHIN 30 DAYS.

Product No.: 0126-10

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